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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
10/039,836	10/23/2001	Virginia C. Crane	35718/239836 (5718-152)	9340

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PIONEER HI-BRED INTERNATIONAL INC.
7100 N.W. 62ND AVENUE
P.O. BOX 1000
JOHNSTON, IA 50131

EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	10

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,836	CRANE ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6*.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of group IV (claims 18-24) in Paper No. 9 is acknowledged. The restriction is made FINAL. Claims 1-17 are withdrawn from consideration as being drawn to nonelected inventions.

2. The disclosure is objected to for the following reasons:

a. Deposit numbers are missing from pg 4, lines 15 and 17, pg 5, line 17, and pg 6, line 16.

b. Embedded hyperlinks and/or other forms of browser-executable code are present on pg 16, line 31. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

3. Several lines of the specification are faint and difficult to read. If Applicant wishes to avoid problems at printing, it is suggested that replacement paragraphs be submitted for the paragraphs starting at the following lines: pg 1, line 1 and 2; pg 10, line 25; pg 14, line 5; pg 30, line 1; pg 30, line 28; pg 34, line 25; pg 65, line 1; and pg 65, line 5.

4. The title of the invention is not descriptive of the instant invention, which is a defense-activated promoter, plants transformed with it, and a method of using it to express a nucleic acid of interest. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

5. The abstract is not descriptive of the instant invention, which is a defense-activated promoter, plants transformed with it, and a method of using it to express a nucleic acid of interest. A new abstract is required that is clearly indicative of the invention to which the claims

are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Claim Objections

6. Claims 23-24 are objected to because of the following informalities:

In claim 23, there is an improper article before "nucleotide" in line 3.

In claim 24, "a stimuli" should be replaced with --a stimulus-- or --stimuli--, as appropriate.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 18-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a promoter of SEQ ID NO:3, constructs comprising that promoter operably linked to heterologous genes, cells and plants comprising the constructs, and methods of using them to induce expression of heterologous genes does not reasonably provide enablement for promoters that have 75% identity to SEQ ID NO:3 or that comprise 20 contiguous nucleotides of SEQ ID NO:3, constructs comprising those promoters operably linked to heterologous genes, cells and plants comprising the constructs, and methods of using them to induce expression of heterologous genes. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to promoters that have 75% identity to SEQ ID NO:3 or that comprise 20 contiguous nucleotides of SEQ ID NO:3, constructs comprising those promoters operably linked to heterologous genes, cells and plants comprising the constructs, and methods of using them to induce expression of heterologous genes.

The instant specification, however, only provides guidance for transformation of maize with ERE-avrRxv, which places control of transcription of the avrRExv gene of the estrogen receptor mRNA and mRNA abundance profiling of the estradiol-induced transgenic plants to show that expression of a proteinase inhibitor-like mRNA is increased when expression of the avr gene is increased (example 1); transient expression of a construct in which the promoter of the proteinase inhibitor-like mRNA (SEQ ID NO:3) is operably linked to GUS in response to HC-toxin and tox+ *Cochiobolus carbonum,* but not in response to tox- *C. carbonum* (example 2); and transient expression of the construct in a cell co-transformed with a nucleic acid encoding maize NPR1 to show that in this situation the promoter is down-regulated (example 2). The specification also provides general guidance for identification of a gene by doing a computer homology search (example 3); general guidance for transformation of maize (examples 4-5), soybean (example 6), and sunflower (example 7); general guidance for performing anti-fungal and anti-bacterial assays (example 8); and general guidance for performing protease inhibition assays (example 9)

The instant specification fails to provide guidance for how proteinase inhibitor-like DNA and its promoter were isolated. The instant specification also fails to provide guidance for exact hybridization or amplification conditions and probes/primers to use in isolation of promoters other than SEQ ID NO:3. The specification fails to teach any 20 contiguous nucleotide segments of SEQ ID NO:3, or segments of any other size, or any nucleic acids with 75% identity to SEQ ID NO:3 that have promoter activity.

Twenty base-pair long regions of a DNA fragment that has promoter activity cannot predictably be assumed to also have promoter activity. Deletion analysis of various promoters have shown that even DNA segments from the portion of a promoter region containing sequence elements thought to be most important (*e.g.*, the TATA-box) need to be longer than 20 basepairs. Maiti et al (1997, Transgen. Res., 6:143-156), in studies on a figwort mosaic virus promoter, found that smallest portion upstream of the transcriptional start site of that would support transcription was 198 basepairs long; segments of 73 and 37 basepairs did not work (Fig. 4). Doelling et al (1995, Plant J. 8:683-692) found that the minimal rRNA promoter of *Arabidopsis thaliana* is at least 33 nucleotides long (Fig. 1).

Identification of the functional parts of promoters is unpredictable. Chen et al (2000, Sex. Plant Reprod. 13:85-94) teach that two promoters with similar expression patterns have major differences in the expression elements required for expression in various flower parts (pg 92, right column, last two paragraphs).

The region of a given promoter that has a specific activity cannot be predicted and involves the complex interaction of different subdomains (Benfrey et al, 1990, Science 250:959-

966, see Abstract, Fig. 3-5). Even a very small region may be critical for activity, and the criticality of a particular region must be determined empirically (Kim et al, 1994, Plant Mol. Biol. 24:105-117, Tables 1-4, Abstract, Fig. 1-2).

Mutation of promoter sequences also produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724).

As the specification does not describe the transformation of any plant with a promoter that has 75% identity to SEQ ID NO:3 or comprises any 20 nucleotide fragment of SEQ ID NO:3, wherein the promoter is operably linked to a heterologous nucleic acid, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those that express the heterologous nucleic acid, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

9. Claims 18-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of promoters that have 75% identity to SEQ ID NO:3 or that comprise 20 contiguous nucleotides of SEQ ID NO:3 and their use. In contrast, the specification only describes a promoter that comprises SEQ ID NO:3. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that promoters that have 75% identity to SEQ ID NO:3 or that comprise 20 contiguous nucleotides of SEQ ID NO:3, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its

> physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 18-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 18 and 21 are indefinite in their recitation of "20 contiguous nucleotide sequences" in lines 8-9 and 11-12, respectively. It is unclear if the claimed nucleic acid comprises 20 copies of SEQ ID NO:3 arranged contiguously or if the nucleotide sequence comprises 20 contiguous nucleotides of SEQ ID NO:3.

Claim 21 lacks antecedent basis for the limitation "said heterologous nucleotide sequence of interest" in lines 10 and 13.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 18-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Perera et al (US Patent 6,462,257, filed 1 June 1999).

Perera et al teach a promoter from pine that comprises 36 contiguous nucleotides of SEQ ID NO:3 (see sequence search results). Perera et al also teach a method of expressing a heterologous nucleic acid in a plant by transformation with an expression vector comprising a construct comprising this promoter operably linked to a heterologous nucleic acid and induction of the promoter with a stimulus and plants thereby obtained (column 6, lines 55-65, claims 8-14 and 19-23). The transformed plants would inherently comprise plant cells transformed with the vector.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
February 21, 2003